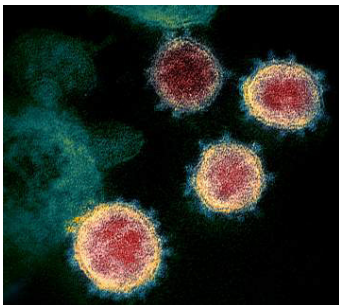


Diagnosis and Management of COVID-19 Disease

SARS-CoV-2 is a novel coronavirus that was identified in late 2019 as the causative agent of COVID-19 (aka coronavirus disease 2019). On March 11, 2020, the World Health Organization (WHO) declared the world-wide outbreak of COVID-19 a pandemic. This document summarizes the most recent knowledge regarding the biology, epidemiology, diagnosis, and management of COVID-19.



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Biology

- SARS-CoV-2 is single-stranded RNA, enveloped virus that likely spread to humans from a zoonotic source, possibly bats or pangolins¹.
- It is believed to spread from **person to person** via **respiratory droplet nuclei**².
- Other routes of infection (e.g. contact, enteric) are possible as the virus can persist on surfaces and is shed in feces, but it is unclear if these are significant means of spread.^{2,3}
- There is evidence of transmission by asymptomatic individuals⁴.
- The virus binds to the ACE2 receptor on type II pneumocytes. However, the role of Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers (ARBs) as treatments or risk factors for disease is unclear⁵.
- The reported incubation time is 3-12 days with a median duration of viral shedding of 20 days^{6,7}.
- There is evidence that the virus changes over time. There may be multiple strains of SARS-CoV-2 in circulation⁸.

Epidemiology

Characteristics such as the **attack rate** (% of individuals in an at-risk population who acquire the infection), **R₀** (R naught, the expected number of cases directly generated by one case in a population where all individuals are susceptible to infection), and **case fatality rate** (CFR, % of infected individuals who die) are contextual. That is, they depend on

factors such as testing rate, population density, and control strategies that vary from location to location. These factors may also change over time. Table 1 summarizes reported epidemiologic characteristics of SARS-CoV-2⁹.

Table 1: Reported epidemiologic characteristics of SARS-CoV-2.

Attack rate:	30-40% (community, in China)
Ro:	2-4 (lower with containment)
Case fatality rate	1.5% USA, 3.4% overall worldwide
Incubation time	3-14 days
Viral shedding	Median 20 days

Clinical Presentation

Symptoms may vary from mild cough to fulminant respiratory failure. Positive tests have also been obtained from asymptomatic patients. Table 2 lists the estimated frequency of symptoms observed to date¹⁰:

Table 2: Frequency of Symptoms in COVID-19

Symptom	Percent of patients with symptom
Cough	50-80%
Fever	85% (only 45% febrile on presentation)
Fatigue	69.6%
Dyspnea	20-40%
URI symptoms	15%
GI symptoms (nausea, vomiting, diarrhea)	10%



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Laboratory Findings

The following lab abnormalities have been observed in patients with COVID-19¹⁰:

- Complete blood count: normal WBC, **leukopenia**, **lymphopenia (80%+)**, thrombocytopenia
- Chemistries: elevated BUN/creatinine, elevated AST, ALT, and Total bilirubin
- Inflammatory markers: normal or low procalcitonin, high C-reactive protein and ferritin
- Miscellaneous: elevated D-dimer, interleukin -6, and lactate dehydrogenase

Imaging:

Imaging findings are frequently absent on presentation and should not be used for diagnosis of COVID. Many patients have normal imaging at the time of presentation, but the following abnormalities have been reported (Figure 1)¹⁰:

- Chest X-ray: bilateral, peripheral, patchy opacities
- Chest CT scan: bilateral ground glass opacities, crazy paving, and consolidation. Not routinely recommended to avoid unnecessary exposure during transport
- Point-of-care ultrasound: B-lines, pleural line thickening, consolidations with air bronchograms. Assessment of cardiac function is also useful

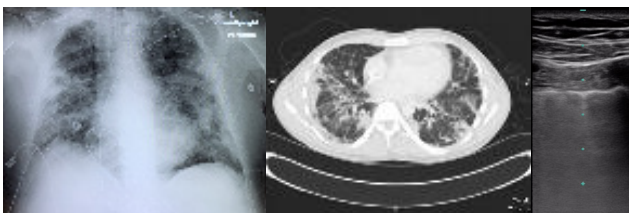


Figure 1: COVID-19 Imaging. (A) CXR showing bilateral peripheral opacities, (B) Chest CT showing diffuse ground glass with a peripheral predominance, (C) point of care lung ultrasound showing predominance of B-lines in patients with COVID-19. Images courtesy of Dr. Nick Mark.

Diagnostic Testing and Reporting:

Lack of availability has hampered testing to date, but testing capacity is increasing quickly. The following recommendations have been made regarding diagnostic testing and reporting^{11,12}.

- Send nasopharyngeal swab for SARS-CoV-2 polymerase chain reaction testing (RT-PCR). Check with your local facility regarding test

characteristics, including sensitivity and specificity

- Differentiating SARS-CoV-2 from other circulating respiratory viruses is important, particularly Influenza, therefore consider testing of usual respiratory pathogens. Co-infection has also been reported
- Do not order sputum induction
- Avoid bronchoscopy unless absolutely indicated
 - ◆ If indicated, follow current recommendations for bronchoscopy in suspected COVID-19 patients as recommended by the American Association for Bronchology and Interventional Pulmonology¹³
- PFTs or spirometry are not indicated in these patients. In addition, ATS and American College of Occupational and Environmental Medicine has recommended against doing routine outpatient PFTs for concerns of spread
- Notify your local health department of positive cases

Isolation and Infection Control for Confirmed and Suspected Cases:

Recommendations for isolation and infection control are evolving as more is learned about the SARS-CoV-2 virus. Current best practices include:

- Place all suspected patients in droplet masks during assessment and when in transit
- If cohorting is required due to resource limitation, keep patients 2 meters apart in a single room
- Restrict visitors
- Try to avoid room entry unless essential; try to move equipment (e.g. IV pumps) out of the room
- Hand hygiene: 20+ seconds with soap and or 60-95% alcohol containing hand gel
- Use appropriate PPE in the correct sequence, including¹⁴:
 - ◆ Standard precautions
 - ◆ Contact precautions
 - ◆ Droplet precautions with eye protection
 - ◆ PLUS airborne precautions for aerosolizing procedures such as intubation, extubation, non-invasive positive pressure ventilation (NIPPV), open circuit suctioning, bronchoscopy, and aerosol treatments

- N95 masks must be fit tested
- All Healthcare professionals must be trained in how to properly don, use, and doff PPE in a manner to prevent self-contamination
- If available, consider powered air-purifying respirator (PAPRs) or controlled air purifying respirators (CAPRs).
 - ◆ Use of tight-fitting respirators require fit testing, but use of loose-fitting respirators does not require fit testing¹⁵

General Treatment Recommendations

The following treatment strategies are recommended based on experience to-date. Of note, these are *suggestions* and should not replace clinical judgement at the bedside.

- Fluid-sparing resuscitation
- Empiric antibiotics if suspicion for secondary infection
- Due to concerns for aerosol spread, nebulizers should be converted to MDIs
- WHO has not recommended against the use of Non-steroidal anti-inflammatory agents. Clinicians should consider alternatives if concerns exist
- Initiating or discontinuing ACE-I and ARBs have been an area of intense discussion. The American College of Cardiology, American Heart Association and Heart Failure Society of America's joint statement recommends against discontinuing ACE-I and ARBs in patients with COVID-19
- Monitor for and treat cardiomyopathy and cardiogenic shock which have been reported as a late complication of COVID-19. Point-of-care ultrasound may be useful in identifying patients with this complication
- Corticosteroids are not recommended except when required for other indications such as asthma or COPD exacerbations, refractory shock or evidence of cytokine storm

Management of Hypoxemic Respiratory Failure

These are *suggestions* and should not replace clinical judgement at the bedside.

- Oxygen by nasal cannula OR simple mask OR non-rebreather masks
- Consider early intubation to avoid use of

- aerosolizing NIPPV and emergent intubations
- Use rapid-sequence intubation. Avoid bag-mask valve if possible due to risk of droplet spread
- Avoid direct laryngoscopy to distance provider from patient. Use video laryngoscopy where possible
- Connect suction and capnography in advance to avoid circuit breaks
- Minimize circuit breaks and use high-efficiency particulate air (HEPA) filters between endotracheal tubes and CO₂ detectors
- Use lung-protective ventilation strategies per ARDSnet protocol. Prone and paralyze as needed
- Patients will likely require a prolonged duration of mechanical ventilation
- Extracorporeal Membrane Oxygenation (ECMO) can be considered but is associated with a high mortality rate¹⁶
- Monitor for and treat **cardiomyopathy** and cardiogenic shock which have been reported as a late complication of COVID-19. Point-of-care ultrasound as well as BNP levels may be useful in identifying patients with this complication
 - ◆ In a recent case series from Washington, 33% of patients developed cardiomyopathy¹⁷

Investigational Therapies

Information on registered clinical trials for COVID-19 in the United States is available at: <https://clinicaltrials.gov/>

- No US Food and Drug Administration (FDA)-approved drugs specifically for the treatment of patients with COVID-19 currently exist. Drugs currently approved for other indications as well as investigational drugs are being studied in clinical trials¹⁷
- FDA approved drugs that may be used off-label
 - ◆ Chloroquine or Hydroxychloroquine—blocks viral entry into the endosome; in vitro data suggests some utility but data from RCTs is lacking
- Investigational agents available in the U.S. Avoid prophylactic use
 - ◆ Remdesivir—anti-viral nucleotide analog
- Other drugs
 - ◆ Lopinavir/ritonavir—anti-viral protease inhibitors; recent negative RCT¹⁹



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- ◆ Tocilizumab—IL-6 inhibitor and may have a role in cytokine storm and for patients in shock

Prognosis

Based on experience in China, 80% of patients have mild symptoms, 15% moderate, and 5% severe (requiring mechanical ventilation). Most patients deteriorate gradually with a median of 9 days from symptom onset to ICU admission. Pregnant women and children appear to have a better prognosis. The following factors have been associated with worse outcomes:

- Increasing age
- Comorbidities including diabetes, cardiovascular disease (including hypertension), and chronic lung disease
- Higher admission sequential organ failure assessment (SOFA) score
- Laboratory abnormalities: elevated D-dimer, ferritin, and troponin

Control Strategies

The following strategies are recommended to slow the rate of SARS-CoV-2 spread:

- Contact tracing
- Social /Physical distancing
- Quarantine of suspected cases and exposed individuals
- Travel restrictions

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